91-1612

No. _____

Supreme Court, U.S.
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In The

Supreme Court of the United States

October Term, 1991

MARY KATHRYN THOMAS,

Petitioner,

v.

HOFFMANN-LaROCHE, INC.,

Respondent.

On Petition For Writ Of Certiorari To The United States Court Of Appeals For The Fifth Circuit

PETITION FOR WRIT OF CERTIORARI

JOHN A. OWENS
P. O. Box 020848
Tuscaloosa, AL 35402-0848
Telephone: (205) 345-5100

Counsel of Record for Mary Kathryn Thomas, Petitioner

Of Counsel:

PHELPS, OWENS, JENKINS, GIBSON & FOWLER
P. O. Box 020848
Tuscaloosa, AL 35402-0848
Telephone: (205) 345-5100

CARTER & DAVIDSON
P. O. Box 981
Columbus, MS 39701
Telephone: (601) 328-2861

COCKLE LAW BRIEF PRINTING CO., (800) 225-6964
OR CALL COLLECT (402) 342-2831

QUESTION PRESENTED

(1) Whether regulation of the prescription drug industry by the Food, Drug and Cosmetic Act and the Food & Drug Administration has preempted state tort law in failure to warn prescription drug cases?

LIST OF PARTIES AND LIST OF PARENT COMPANIES AND SUBSIDIARIES

Pursuant to Rules 14.1(b) and 29.1 of the *Rules of the Supreme Court of the United States*, Petitioner states as follows:

Petitioner is Mary Kathryn Thomas, Plaintiff/Appellant below.

Respondent is Hoffmann-La Roche, Inc. (hereinafter Roche), Defendant/Appellee below. Upon information and belief, Roche is a corporation organized and existing under the laws of the state of New Jersey, with its principal place of business in Nutley, New Jersey. Its parent company is F. Hoffmann-La Roche, Ltd. of Basle, Switzerland. Its affiliates or subsidiaries are Roche Diagnostic Systems, Inc.; Hoffmann-La Roche Service Corporation; Hoffmann-La Roche Sciences, Inc.; Lab Delivery Service of New York City, Inc.; Medi-Physics, Inc.; Rorad, Inc.; Technad, Inc.; Cintichem, Inc.; Roche Professional Service Centers, Inc.; Hoffmann-La Roche Enterprises, Inc.; Roche Medical Electronics, Inc.; Hoffmann-La Roche Holdings, Inc.; Roche Biomedical Laboratories, Inc.; Analytics Laboratory, Inc.; Medical Laboratory Associates, Inc.; Sacramento Clinical Laboratory, Inc.; Columbus Pathology Laboratory, Inc.; Kontron Electronics, Inc.; and The Hoffmann-La Roche Foundation.

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No. _____

In The

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MARY KATHRYN THOMAS,

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v.

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Respondent.

On Petition For Writ Of Certiorari To The United States Court Of Appeals For The Fifth Circuit

PETITION FOR WRIT OF CERTIORARI

TO: The Honorable, the Chief Justice and Associates Justices of the Supreme Court of the United States:

Mary Kathryn Thomas, the Petitioner herein, prays that this Court issue its Writ of Certiorari and summarily reverse the judgment of the United States Court of Appeals for the Fifth Circuit entered in the above-captioned case on 3 January 1992, Rehearing Denied on 25 February 1992.

OPINIONS BELOW

On 29 June 1989, judgment was entered in accordance with the jury's findings for Mary Kathryn Thomas after

trial in the United States District Court for the Northern District of Mississippi. Thereafter, on 16 November 1989, the Trial Judge, the Honorable Glen H. Davidson, entered judgment notwithstanding the verdict in the United States District Court for the Northern District of Mississippi, which is reported as *Thomas v. Hoffmann-La Roche, Inc.*, 731 F. Supp. 224 (N.D. Miss. 1989).

The United States Court of Appeals for the Fifth Circuit affirmed the Trial Court's entry of judgment notwithstanding the verdict on 3 January 1992, by an as yet unreported opinion, a copy of which is printed as Appendix A hereto.

Mary Kathryn Thomas's Petition for Rehearing and Suggestion of Rehearing En Banc were denied on 25 February 1992. A copy of that denial is printed as Appendix B hereto.

JURISDICTION

The opinion of the United States Court of Appeals for the Fifth Circuit affirming the Trial Court's judgment below was entered on 3 January 1992. A timely petition for Rehearing and Suggestion of Rehearing En Banc was filed and they were denied on 25 February 1992. The jurisdiction of the Supreme Court is invoked pursuant to 28 U.S.C. §2101(c).

Jurisdiction in the United States Court of Appeals for the Fifth Circuit was based upon 28 U.S.C. §1291.

Jurisdiction in the United States District Court for the Northern District of Mississippi was based upon 28

U.S.C. §1332, diversity of citizenship with an amount in controversy which exceeded Ten Thousand ($10,000.00) Dollars (the jurisdictional amount in January of 1986).

STATUTORY PROVISIONS INVOLVED

Article VI of the Constitution of the United States provides in relevant part:

* * *

> This Constitution, and the laws of the United States which shall be made in pursuance thereof; and all treaties made, or which shall be made, under the authority of the United States, shall be the supreme law of the land; and the judges in every state shall be bound thereby, any thing in the Constitution or laws of any state to the contrary notwithstanding.

* * *

Title 21 of the *Code of Federal Regulations* §314.70 provides in relevant part:

> Supplements and other changes to an approved application.
>
> * * *
>
> (b) Supplements requiring FDA approval before the change is made.
>
> * * *
>
> (3) Labeling. Any change in labeling, except one described in paragraph (c)(2) or (d) of this section.

* * *

(c) Supplements for changes that may be made before FDA approval.

* * *

(2) Changes labeling to accomplish any of the following:

(i) To add or strengthen a contraindication, warning, precaution, or adverse reaction;

* * *

Title 21 of the *Code of Federal Regulations* §601.12 provides in relevant part:

Changes to be reported.

(a) General. Important proposed changes in location, equipment, management and responsible personnel or in manufacturing methods and labeling, of any product for which a license is in effect or for which an application for license is pending, shall be reported to the Director, Center for Biologics Evaluation Research, by the manufacturer, and unless in case of an emergency, not less than 30 days in advance of the time such changes are intended to be made.

* * *

STATEMENT OF THE CASE

Mary Kathryn Thomas was the Plaintiff in a medical malpractice and products liability action filed in the United States District Court for the Northern District of

Mississippi, Eastern Division, in January of 1986, wherein she claimed damages for injuries sustained as a result of the use of the prescription drug Accutane. A pro tanto settlement was reached with Dr. Robert P. Myers, the prescribing physician, in February of 1988 and he was dismissed from the case.

After a long and acrimonious discovery process, the matter was tried to a jury in June of 1989; Ms. Thomas was awarded $1,000,000 in damages by the jury; and, judgment was entered on 29 June 1989 by the trial court. On 7 July 1989, Roche filed a motion for judgment notwithstanding the verdict or in the alternative for a new trial. On 16 November 1989, the trial judge entered judgment notwithstanding the verdict. On 1 December 1989, Ms. Thomas filed notice of appeal in the trial court invoking the jurisdiction of the United States Court of Appeals for the Fifth Circuit. On 3 January 1992, the Court of Appeals affirmed the Trial Court's entry of judgment notwithstanding the verdict. On or about 23 January 1992, Ms. Thomas filed a Petition for Rehearing and a Suggestion of Rehearing En Banc, both of which were denied on 25 February 1992.

STATEMENT OF THE FACTS

Dr. Robert Myers prescribed Accutane for Mary Kathryn Thomas in January of 1984 for a skin condition.[1]

[1] The evidence in the Record supports a finding that Ms. Thomas did not have severe recalcitrant cystic acne.

She immediately began experiencing adverse effects, ultimately becoming disoriented. Dr. Myers took her off Accutane but her condition required repeated hospitalizations over the next few months. She suffered from headaches, confusion, disorientation, multiple grand mal seizures and coma.

Prior to the time Ms. Thomas was injured, Roche never warned of the risk of seizures or comas associated with the use of the drug Accutane, which had first been marketed in September of 1982 after testing in only 523 patients.

After a long and thorough qualification process, Dr. James O'Donnell testified at trial that Accutane causes seizures in some people and that it caused Ms. Thomas's seizures. Ms. Thomas's treating physician also testified that Accutane caused her injuries. There was no evidence whatsoever presented by Roche to prove that Accutane cannot cause seizures. None of Roche's experts were able to identify a specific causal agent.

Roche ultimately (long after Ms. Thomas's injuries) included a warning in the package insert that accompanies Accutane which merely mentioned seizures. However, no evidence of that subsequent warning was admitted at the trial because of Roche's objections. The only language Dr. Myers had arguably seen associating Accutane with seizures at the time he prescribed it for Ms. Thomas was an obscure reference to seizures in Accutane therapy in the *Journal of the American Academy of Dermatology* published in October of 1983. However, Dr. Myers was confused and his testimony on this and other matters was equivocal.

Dr. O'Donnell testified that the warning ultimately given was inadequate for a number of reasons making Accutane unreasonably dangerous. He testified that the warning was inadequate at the time Accutane was prescribed for Ms. Thomas because no warning of seizures was given by Roche, even though it was aware that comas and seizures had been associated with Hypervitaminosis A (Accutane is an analog of Vitamin A); there had been a seizure in Accutane clinical trials; and, ten seizure reports in Accutane patients had been received by Roche at that time. He also testified that the reference to seizures which was ultimately added to the package insert and the *Physician's Desk Reference* was inadequate in content in that the warning, which stated that seizures have been reported but "may bear no relationship to therapy", should have affirmatively noted that seizures are associated with Accutane; that use of the drug may cause symptoms consistent with Hypervitaminosis A; and that the indication for usage be in cases of severe recalcitrant cystic acne only, the only use for which Accutane has ever been approved by the FDA. Dr. O'Donnell also stated that the warning that was ultimately given was inadequate in the way it was presented.

Most significantly to this Petition, however, is that Dr. O'Donnell testified that in his opinion Accutane should be contraindicated for any condition other than severe recalcitrant cystic acne. Dr. O'Donnell held this opinion because of the severe side effects associated with Accutane and because of the history of gross overuse of the drug for other conditions. The Fifth Circuit Court of Appeals upheld the trial court's judgment notwithstanding the verdict because it felt that the plaintiff had failed

to prove that the prescribing physician, even given an adequate warning, would not have prescribed the drug for Ms. Thomas or would have done something differently. If the contraindication testimony stood then necessarily the jury verdict should have been affirmed because Dr. Myers himself and all other physicians in the case who testified on the point were unequivocal that doctors do not and should not prescribe within a contraindication except in life or death or similar drastic circumstances. The jury obviously found that Ms. Thomas did not have severe recalcitrant cystic acne and, therefore, that Dr. Myers would not have prescribed Accutane for her if the contraindication advocated by Dr. O'Donnell had been given. Thus, if the trial court had not improperly decided that Dr. O'Donnell's testimony was not substantial evidence because of an FDA preemption theory, the jury verdict would have been affirmed.

ARGUMENT

REGULATION OF THE PRESCRIPTION DRUG INDUSTRY BY THE FOOD, DRUG AND COSMETIC ACT AND THE FOOD & DRUG ADMINISTRATION DOES NOT PREEMPT STATE TORT LAW IN FAILURE TO WARN PRESCRIPTION DRUG CASES.

The United States Court of Appeals for the Fifth Circuit stated in its opinion:

> If we permit the subjective opinion of a single expert to create a genuine issue of material fact in the face of the decisions of the FDA and thousands of physicians so that a particular plaintiff can recover, we would be denying

> access to Accutane for hundreds of thousands of acne suffers.

Thomas v. Hoffmann-La Roche, Inc., at 1457. See Appendix A, App. 23. The Fifth Circuit is in essence holding that the Food, Drug and Cosmetic Act[2] and the Food & Drug Administration (FDA) which regulate prescription drugs and which approved the deficient warning which was in the Accutane package insert have preempted the pharmaceutical field to the exclusion of the judicial system and, therefore, that Ms. Thomas's cause of action in products liability based on a claim of inadequate warning is effectively preempted. The court concluded that the manufacturer's failure to include the contraindication recommended by Ms. Thomas's expert, Dr. James O'Donnell, did not render the warning inadequate because the FDA had never mandated such a contraindication.

Not only does the Fifth Circuit's opinion constitute a finding that regulation of the pharmaceutical field by the FDA has effectively preempted state tort law but it recognizes a preemption by negative inference. The Court of Appeals is saying that because the FDA never required such a contraindication – indeed, it never even considered such a contraindication because one was never suggested by the manufacturer – that the failure to include it cannot even be examined for reasonableness. This is absolutely contrary to this Court's holding in *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 104 S.Ct. 615, 78 L.Ed.2d 443 (1984).

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[2] 21 U.S.C. §§301 et seq.

In the courts below, the manufacturer cited *Hurley v. Lederle Laboratories Division of American Cyanamid Co.*, 863 F.2d 1173 (5th Cir. 1988) for the proposition that the pharmaceutical field has been preempted by the FDA. However, in *Hurley* the injury causing product at issue was a vaccine not a prescription drug such as Accutane. The Fifth Circuit did hold in *Hurley* that once the manufacturer has provided the FDA with the information necessary to determine the contents of a vaccine package insert, juries are not free to determine the adequacy of that prescribing information. However, the regulation at issue in *Hurley*, specifically 21 C.F.R §601.12, permits the manufacturer of the vaccine to change the language in such product inserts only *with* FDA approval and applies to vaccines only, whereas the regulations with respect to labelling applicable to a drug such as Accutane, specifically 21 C.F.R. §314.70(b)(3) and 21 C.F.R. §314.70(c)(2)(i), allow changes to labelling to add or strengthen a warning *without* prior approval of the FDA.

The preemption notion arises from the Supremacy Clause of the United States Constitution. U. S. Constitution, Article VI, Clause 2. Federal preemption can occur where Congress expressly preempts state law; inferentially preempts state law through the comprehensiveness of a federal regulatory scheme; or, where a regulatory scheme does not entirely displace state regulation in an area, state law which actually conflicts with the federal law is preempted, i.e. compliance with both federal and state regulation is a physical impossibility.

In *Osburn v. Anchor Laboratories, Inc.*, 825 F.2d 908 (5th Cir. 1987), the Fifth Circuit expressly rejected the preemption argument where regulations specifically permitted

the manufacturer to add supplemental warnings to a previously approved label, as soon as the manufacturer became aware of the need to do so, without first obtaining approval from the FDA. In *Osburn*, the product at issue was a veterinary prescription drug. The Fifth Circuit based its holding upon the fact that the FDA regulations at issue there specifically permitted the addition of warnings to a previously approved label as soon as necessary without prior FDA approval of the supplemental warnings. Consequently, the court concluded that federal law neither made it practically nor legally impossible to give the warnings which state tort law would find adequate. Accutane is just such a drug. Therefore, in finding preemption, the Fifth Circuit has not followed the law established in that Circuit.

Nowhere is the "preemption due to regulation" argument more clearly eviscerated than in *Silkwood v. Kerr-McGee Corp.*, 464 U.S. 238, 104 S.Ct. 615, 78 L.Ed.2d 443 (1984), in which this Court held that Congressional intent to preempt must be absolutely clear before preemption will be found. In that case, this Court found that extensive regulation of nuclear energy by the federal government did not result in preemption of a state law cause of action. *Also see, Hillsborough County v. Automated Medical Laboratories, Inc.*, 471 U.S. 707, 105 S.Ct. 2371, 85 L.Ed.2d 714 (1985). As these cases clearly illustrate, the Fifth Circuit has also failed to follow the law of this Court.

In *Abbott v. American Cyanamid Company*, 844 F.2d 1108 (4th Cir. 1988), the Fourth Circuit stated that preemption does not necessarily follow from comprehensive federal regulation of prescription biological products. The overall goal of the Food, Drug and Cosmetic Act is the

safety of drugs and biological products, and that goal is more enhanced than frustrated by state tort law. *Id.* at 1113. The *Abbott* court also acknowledged that the Vaccine Compensation Amendments of 1987 expressly deny Congress's intent to preempt the pharmaceutical field.

Numerous decisions have found the regulations of the FDA to establish minimum standards and have found that state law may set higher standards for due care and safety. *Allen v. G. D. Searle & Co.*, 708 F.Supp. 1142 (D.Or. 1989); *Wooderson v. Ortho Pharmaceutical Corp.*, 235 Kan. 387, 681 P.2d 1038, *cert. denied*, 469 U.S. 965, 105 S.Ct. 365, 83 L.Ed.2d 301 (1984); *Brochu v. Ortho Pharmaceutical Corp.*, 642 F.2d 652 (1st Cir. 1981). In *Feldman v. Lederle Laboratories*, 97 N.J. 429, 479 A.2d 374 (1984), the court held that the Food, Drug and Cosmetic Act and the FDA regulation of prescription drug labeling does not preempt state tort law actions for failure to adequately warn of the dangers of the prescription drug Tetracycline.

In *R. J. Reynolds Tobacco Company v. Durham County, North Carolina*, 479 U.S. 130, 107 S.Ct. 499, 93 L.Ed.2d 449 (1986), this Court stated that federal regulation of a field should not be deemed preemptive of state regulatory power unless the nature of the regulated subject permits no other conclusion or unless Congress has unmistakably preempted the field. *Also see Florida Lime & Avocado Growers, Inc. v. Paul*, 373 U.S. 132, 83 S.Ct. 1210, 10 L.Ed.2d 248 (1963); *Merrill Lynch, Pierce, Fenner & Smith, Inc. v. Ware*, 414 U.S. 117, 94 S.Ct. 383, 38 L.Ed.2d 348 (1973); *Ferebee v. Chevron Chemical Co.*, 736 F.2d 1529 (D.C. Cir)., *cert. denied*, 469 U.S. 1062, 105 S.Ct. 545, 83 L.Ed.2d 432 (1984).

In *Graham v. Wyeth Laboratories*, 666 F.Supp. 1483 (D. Kan. 1987),[3] the court noted that Congress had recently clarified its intent that FDA regulations should not preempt state tort law remedies even for victims of vaccine-related injuries.[4] That court also reiterated that FDA regulations regarding prescription drugs are generally viewed as setting minimum standards, both as to design and warning, and held that in the absence of express preemption, there is a strong presumption that Congress did not intend to displace state law. Citing the enactment of the National Childhood Vaccine Injury Act in November of 1986,[5] the court found that Congress had clearly evidenced a willingness to allow state tort remedies for vaccine-related injuries, despite *broad* federal regulation and despite a manufacturer's compliance with such regulation. *Id.* at 1492. The court also noted that the majority of federal courts which have considered the issue of implied preemption in the case of vaccine regulations have found that there is no such implied preemption of state tort law remedies. *Id.* at 1493. *Also see, Ferebee v. Chevron Chemical Co.*, 736 F.2d 1529 (D.C.Cir.), *cert. denied*, 469 U.S. 1062, 105 S.Ct. 545, 83 L.Ed.2d 432 (1984); *Callan v. G. D. Searle & Co.*, 709 F.Supp. 662 (D. Md. 1989). In *McEwen v. Ortho Pharmaceutical Corp.*, 270 Or. 375, 528

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[3] *See also, Graham v. Wyeth Laboratories*, 706 F.2d 1399, 1405 n.9 (10th Cir. 1990).

[4] As noted above, the regulations pertaining to vaccines are much more restrictive than those for drugs such as Accutane.

[5] 42 U.S.C. §300aa-22, an amendment to the Public Health Service Act of November 14, 1986, Pub. L. No. 99-660, 100 Stat. 3743.

P.2d 522 (1974), the court held that warnings given by a drug manufacturer may be found inadequate even if all governmental regulations have been followed. *Also see, Yarrow v. Sterling Drug, Inc.*, 263 F.Supp. 159 (D.S.D. 1967), *aff'd*, 408 F.2d 978 (8th Cir. 1969).

There is absolutely no evidence in the Record that the contraindication advocated by Dr. O'Donnell, which he testified would have made the manufacturer's warning which accompanied Accutane adequate, was ever mentioned to or considered by the FDA. Nor is there any evidence in the Record that the manufacturer ever asked for but was denied permission to add seizure and coma adverse effect warnings to the package insert before Ms. Thomas was injured. Any negative inference that the FDA's failure to affirmatively seek inclusion of such warning or contraindication is somehow a preemption of Mary Kathryn Thomas's right to seek judicial remedy constitutes a blatant misapplication of the law.

The Panel's cursory conclusion that the FDA had decided no contraindication was needed is without any support. The FDA approved Accutane only for use in severe recalcitrant cystic. When polled, two of the seven members of the Dermatologic Advisory Committee, which ultimately recommended Accutane for marketing, voted against approval of the drug on safety grounds. Because the FDA did require the contraindication of the drug for certain patients, the Fifth Circuit presumes by negative inference that the FDA determined that contraindication in less severe forms of acne is unwarranted. Even if the FDA did affirmatively decide against contraindication, a holding that this precludes testimony by a duly qualified expert to the contrary is nothing but the

adoption of the preemption argument made by the manufacturer in the lower court. Such a conclusion completely discounts not only the evidence presented in this case but well-founded precedent of this Court and the lower federal courts, including the Fifth Circuit, and will result in diminished accountability of the FDA for the health and safety of the citizens of this country.

CONCLUSION

For the foregoing reasons, Mary Kathryn Thomas respectfully requests that her Petition for Writ of Certiorari be granted.

Dated 6 April 1992.

Respectfully submitted,

JOHN A. OWENS

Counsel of Record for
Mary Kathryn Thomas

Of Counsel:

PHELPS, OWENS, JENKINS, GIBSON & FOWLER
P.O. Box 020848
Tuscaloosa, AL 35402-0848
Telephone: (205) 345-5100

CARTER & DAVIDSON
P.O. Box 981
Columbus, MS 39701
Telephone: (601) 328-2861

APPENDIX A

Decision of the United States Court of Appeals for the Fifth Circuit affirming Judgment Notwithstanding the Verdict, dated 3 January 1992.

Mary Kathryn THOMAS,
Plaintiff-Appellant,

v.

HOFFMAN-LaROCHE, INC.,
Defendant-Appellee.

No. 89-4908.

United States Court of Appeals,
Fifth Circuit.

Jan. 3, 1992.

Patient brought products liability action against manufacturer of acne drug, alleging failure to warn of risk of seizures. The United States District Court for the Northern District of Mississippi, Glen H. Davidson, J., 731 F.Supp. 224, granted judgment notwithstanding verdict for manufacturer, and appeal was taken. The Court of Appeals, Wisdom, Circuit Judge, held that, even if manufacturer's failure to inform physicians of possibility of seizures at earliest possible data rendered drug unreasonably dangerous, manufacturer was not liable to patient who suffered seizures absent showing that adequate warning would have prevented patient's injury.

Affirmed

Appeal from the United States District Court for the Northern District of Mississippi.

Before WISDOM, KING and BARKSDALE, Circuit Judges.

WISDOM, Circuit Judge:

Mary Kathryn Thomas sued Hoffman-LaRoche, Inc., the manufacturer of a prescription acne medication called Accutane, under a failure to warn theory[1] for injuries she sustained allegedly as a result of taking Accutane. The district court granted Hoffman-LaRoche's post-trial motion for judgment notwithstanding the verdict, setting aside a jury award of one million dollars. The district court held that Thomas had failed to introduce sufficient evidence to show that the allegedly inadequate warning caused her injury. 731 F.Supp. 224. We AFFIRM.

I. FACTUAL AND PROCEDURAL BACKGROUND

A. *The Injury.*

In late January 1984, the plaintiff had an appointment with her dermatologist, Dr. Robert P. Myers. She had been under Dr. Myer's treatment since 1979 for acne rosacea. When she met with Dr. Myers, Dr. Myers diagnosed Thomas as having developed a more serious form of acne, cystic acne. The cystic acne had proved resistant to the antibiotic treatment that Dr. Myers had prescribed

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[1] Thomas alleged both that Hoffman-LaRoche was negligent for failing to warn and that the product Accutane was unreasonably dangerous because of the inadequacy of the warning. We consider both the negligence and the strict liability action together. Thomas also alleged a breach of express warranty, which issue is not before us on appeal.

for Thomas's acne rosacea, so Dr. Myers decided to prescribe Accutane for Thomas. At a monthly check-up on February 23rd, Thomas reported experiencing dry skin and headaches as side effects of the Accutane. Dr. Myers prescribed a skin cream for the dry skin, but, because of success in treating Thomas's acne, maintained Thomas's Accutane treatment.

Several days later Dr. Myers received a telephone call from Thomas's daughter who told Dr. Myers that her mother was disoriented and confused. Dr. Myers met with Thomas the following day, took her off Accutane, and referred her to a local internist, Dr. Dill. Dr. Dill, in turn, referred Thomas to Dr. Lawrence Mahalak, a neurologist. Thomas was hospitalized on February 29, 1984, suffering from a fever and disorientation.

On March 6th, Thomas was transferred to the Mayo Clinic in Rochester, Minnesota. While at the Mayo Clinic, March 12th, Thomas suffered her first seizure. She recovered from her fever and was discharged on March 23rd. On discharge, Dr. William Swanson, the treating physician at the Mayo Clinic during her March stay, wrote that the cause of her illness was "uncertain although the course [of her illness] would be most compatible with some type of infectious etiology, most likely viral."

On May 16th, Thomas was again admitted to a local hospital, under the care of Dr. Mahalak, suffering from a fever and disorientation. She was diagnosed as having pneumonia. While in the hospital, Thomas suffered her second seizure. She was transferred to the Mayo Clinic on May 22nd. At the time of her transfer, Dr. Mahalak, in

consultation with Dr. William Causey, an infectious disease expert, attributed the seizures to a recurrent central nervous system infection. Thomas recovered and was released from the Mayo Clinic on May 26th. At the time of her discharge from the Mayo Clinic, the neurologist in charge of her treatment, Dr. J.D. Bartleson, stated that he was unable to reach a diagnosis.

In early June 1984, Thomas, again suffering from fever and disorientation, was admitted to the University of Southern Alabama Hospital under the care of Dr. William Kase, a board certified neurologist. She recovered from her symptoms and was released within four days.

In February of 1989, Thomas, again suffered from fever and disorientation, was admitted to a local hospital under the care of Dr. Mahalak. While in the hospital, she suffered a third seizure. Every expert who testified as to the cause of the 1989 seizure agreed that it was most likely caused by a virus, though a specific virus was neither isolated nor identified. The experts who expressed an opinion on the issue agreed that this third seizure was not related to the taking of Accutane in 1984.[2]

At trial, Thomas introduced the testimony of three experts to establish that her use of Accutane had caused

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[2] Thomas contends that Accutane caused her to develop a seizure disorder and that she would suffer recurrent seizures because of her month-long treatment with Accutane. There is no competent evidence in the record to establish that Accutane could cause such a disorder.

her 1984 seizures. Dr. O'Donnell,[3] an expert with a Ph.D. in Pharmacy, testified that he believed that Accutane did cause seizures in some patients, though he was not permitted to express his opinion as to whether the use of Accutane caused Thomas's seizures. Two physicians, Dr. Mahalak and Dr. William J. Riley,[4] testified that, to a reasonable degree of medical certainty, Accutane had caused Thomas's two 1984 seizures.

Hoffman-LaRoche introduced Thomas's contemporaneous medical records, and the testimony of four other physicians, Dr. Causey, Dr. Kase, Dr. Swanson, and Dr. Elias Chalhub.[5] The records and the testimony introduced by Hoffman-LaRoche consistently pointed to an infectious process as the most likely cause of Thomas's fevers and seizures.

Despite the fact that over a million patients had used Accutane at the time of trial, no epidemiological study

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[3] Dr. O'Donnell was not involved in the treatment of Thomas, but was hired by her attorneys in anticipation of litigation. He was qualified, by the district court, as an expert in the field of medical warnings. Dr. O'Donnell testified that he was receiving between ten and fifteen thousand dollars for his testimony in this case, and that he was providing similar testimony in twelve other cases.

[4] Dr. Riley also was hired in anticipation of trial. He had never examined Thomas, and expressed his opinion based on a brief review of her medical record. At the time Dr. Riley expressed his opinion, he did not have available information on the 1989 seizure. Several of the experts testified that the 1989 seizure was an important consideration in determining the likely cause of the 1984 seizures.

[5] Dr. Chalhub was not involved in the treatment of Thomas, but was hired in anticipation of trial.

was presented that would suggest a causal connection between Accutane and seizures. One epidemiological study was completed and available at the time of trial, but neither party introduced the study.

B. *The Warning Evidence.*

Before Dr. Myers prescribed the drug, Hoffman-LaRoche had made available to him information that the product had been effective in treating patients with acne, but warned that a number of side effects were common. With respect to Accutane, the 1983 version of the Physician's Desk Reference ("PDR") stated:

> Because of significant adverse effects associated with its use, Accutane should be reserved for patients with severe cystic acne who are unresponsive to conventional therapy, including systemic antibiotics.

In addition to this general warning, the PDR description also warned of a number of specific side effects that had been observed in Accutane patients: cheilitis, conjunctivitis, musculoskeletal symptoms, rash, temporary thinning of hair, skin peeling, skin infections, nonspecific urogenital findings, nonspecific gastrointestinal symptoms, fatigue, headache, and increased susceptability to sunburn. The 1983 PDR description noted that use of Accutane was contraindicated for pregnant women and for patients who are sensitive to parabens.[6] By January 1984, Hoffman-LaRoche had also provided specific warnings by letter concerning three other side effects observed

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[6] Parabens are used as a preservative in Accutane.

in Accutane patients: pseudotumor cerebri, corneal opacities, and skeletal hyperostosis.[7] The company provided the same information in inserts in the packages containing the product. The plaintiff seeks recovery arguing that Accutane was unreasonably dangerous despite these extensive warnings because Hoffman-LaRoche failed to list seizures as one of the potential side effects.

The testimony at trial established that, at the time Dr. Myers prescribed Accutane for the plaintiff's acne condition, doctors had prescribed Accutane to some four hundred thousand patients, of whom nine had reported "seizures"[8] after using Accutane. A tenth seizure was reported to Hoffman-LaRoche in late January of 1984, several days after the plaintiff began her Accutane treatment. The evidence further established that, by May of 1989, over a million patients had been treated with Accutane. Forty-nine seizures had been reported.

Hoffman-LaRoche received these reports and forwarded them to the Food and Drug Administration. Because it was unclear whether these seizures were caused by the use of Accutane, Hoffman-LaRoche did not specifically mention seizures in its warning at the time Dr. Myers prescribed Accutane for the plaintiff. Hoffman-LaRoche added a reference to seizures in the 1985PDR,

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[7] Some of these side effects had been observed only when Accutane was used to treat a patient with a disorder of Keratinization, and had not been observed when Accutane was used to treat acne patients.

[8] The "seizure" reports ranged from incidents that resembled fainting to grand mal seizures.

and sent a "Dear Doctor" letter[9] in the spring of 1984, notifying physicians of the change in the PDR description. Even in the spring of 1984, it remained unclear whether these incidents were caused by the use of Accutane; as a result, Hoffman-LaRoche's warning stated only that seizures "ha[d] been reported in less than one percent of patients and may bear no relation to treatment".

At trial, Thomas presented the testimony of Dr. O'Donnell to support her position that the warning accompanying Accutane was inadequate and that an adequate warning would have prevented her injury. Dr. O'Donnell testified that the warning given by Hoffman-LaRoche was inadequate for two reasons. First, Hoffman-LaRoche should have warned of the possibility of a slight risk of seizures associated with the use of Accutane in the fall of 1983, instead of in the spring of 1984. Second, because of the overall level of risk associated with Accutane, the warning should have stated that use of the product is contraindicated for all patients other than those with severe cystic acne.[10]

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[9] When a drug company discovers new information concerning side effects or possible adverse reactions to one of its products, the company typically sends a letter to physicians relating the new information. This letter is referred to as a "Dear Doctor" letter.

[10] Dr. O'Donnell further testified that the warning remained inadequate despite the seizure language added by Hoffman-LaRoche in the spring of 1984. He testified that the warning should have read: "seizures have been associated with [Accutane] and may or may not bear relationship to therapy".

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With regard to whether an adequate warning would have changed Dr. Myers's decision to use Accutane, Dr. O'Donnell first testified:

> In my opinion, if the warnings were complete as I described them and the use in less than severe conditions of acne was contraindicated, a reasonable physician would not have prescribed [Accutane] for Mrs. Thomas.

Counsel for Hoffman-LaRoche objected, on the basis that the opinion assumed a diagnosis of Thomas's condition that was not supported by any credible evidence.[11] The trial judge sustained the objection, but, after discussion, permitted Dr. O'Donnell to testify on the issue, provided

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We find untenable his suggestion that any reasonable physician would read his "associated with" and "may or may not bear relationship" language different from Hoffman-LaRoche's "have been reported in" and "may bear no relationship" language. Both warnings substantively connote the same thing: seizures have been observed in patients during the Accutane treatment period, and it is uncertain whether the seizures were caused by Accutane or coincidental.

[11] Dr. Myers testified, and Thomas's contemporaneous medical records reflect, that Thomas was suffering from cystic acne in January of 1984, when Dr. Myers prescribed Accutane. Dr. Myers testified that, in 1980, Thomas had a less severe form of acne – acne rosacea. Both Thomas and her daughter, testified that they did not know Thomas had cystic acne in 1984. Thomas also elicited testimony from Dr. Myers that one generally knows if one has cystic acne. From this, Thomas argues that a reasonable jury could have inferred that Thomas did not have cystic acne in 1984, but was suffering from acne rosacea.

that he not refer to a diagnosis unsupported by the evidence. Dr. O'Donnel did so:

> Q. Doctor, do you have an opinion as to what a reasonably knowledgeable physician, as to whether or not a reasonably knowledgeable physician who was given the warnings that you have told the jury you thought should have been in effect for Accutane in January of 1984, whether a reasonable physician so warned would have prescribed Accutane to Mrs. Thomas?
>
> A. I do have an opinion, sir.
>
> Q. And what is that opinion?
>
> A. A reasonable physician would not have prescribed the Accutane for Mrs. Thomas.

Dr. Myers, on the other hand, testified that he had read in the fall of 1983 of the possibility that Accutane may have caused seizures in very rare cases. He further testified that he would not have changed his decision if warned of the possible risk of seizure.

C. *Resolution of the Issues at Trial.*

The case was submitted to the jury, and the jury returned a judgment in favor of Thomas in the amount of one million dollars. Hoffman-LaRoche moved for a judgment notwithstanding the verdict, or alternatively for a new trial. In resolving the motion, the trial judge held that a plaintiff must prove two facts to establish that a failure to warn of a risk associated with a prescription drug caused the plaintiff's injury. First, he held that a plaintiff must demonstrate that an adequate warning

would have changed the treating physician's decision to prescribe the drug for the plaintiff. Second, he held that a plaintiff must also show that the drug caused the plaintiff's injuries. The trial judge held that there was insufficient evidence to support a finding in favor of the plaintiff, and granted Hoffman-LaRoche's motion for judgment notwithstanding the verdict.

II. ADEQUACY OF WARNING

Under Mississippi law,[12] a product may be unreasonably dangerous if the manufacturer fails to warn of a non-obvious risk associated with the normal use of the product. When the product in question is a prescription drug, such as Accutane, Mississippi follows the learned intermediary doctrine.[13] Under this doctrine, the manufacturer's failure to warn the patient of the product's risks does not render the product defective or unreasonably dangerous so long as the manufacturer adequately warns the learned intermediary.[14] Both parties agree that Thomas bears the full burden of establishing that Accutane was the cause of her 1984 seizures.[15] They disagree over whether Mississippi law requires the plaintiff to establish that an adequate warning would have changed Dr. Myers's decision to prescribe Accutane for Thomas.

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[12] Both parties agree that Mississippi substantive law governs our analysis in this diversity action.

[13] *Wyeth Labs., Inc. v. Fortenberry,* 530 So.2d 688, 691-92 (Miss. 1988).

[14] 530 So.2d at 691-92.

[15] The parties do disagree over whether the evidence was sufficient to support such a finding.

In resolving this dispute, we begin with the Mississippi Supreme Court's recent decision in *Wyeth Laboratories, Inc. v. Fortenberry.*[16]

A. *Inadequate Warning and Causation.*

In *Fortenberry,* the plaintiff brought suit, against his doctor and Wyeth Laboratories, alleging injuries caused by a non-swine influenza vaccine. The plaintiff alleged that the product was unreasonably dangerous because of an inadequate warning.[17] The *Fortenberry* Court rejected his claim, finding that the warning was adequate as a matter of law.[18] The *Fortenberry* Court also addressed whether a plaintiff must establish causation:

> Assuming arguendo that the warning was inadequate, Fortenberry still had the burden of showing that an adequate warning would have altered Dr. Moore's conduct.[19]

Thomas characterizes this statement as dictum and urges us to ignore it. We cannot do so. Under diversity jurisdiction, considered dictum stating how an issue is to be resolved is evidence we must consider in determining the most likely result to be reached by a Mississippi court faced with this issue.[20] Given that no other Mississippi court has spoken on the subject, we consider this plain

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[16] 530 So.2d 688 (Miss. 1988).

[17] 530 So.2d at 691.

[18] 530 So.2d at 692-93.

[19] 530 So.2d at 691.

[20] *See, e.g., Towne Realty, Inc. v. Safeco Ins. Co. of America,* 854 F.2d 1264, 1269 n. 5 (11th Cir.1988).

and unconditioned statement by the *Fortenberry* Court to be convincing evidence of the likely result under Mississippi law. We, therefore, hold that, under Mississippi law, in a prescription drug failure to warn case, the plaintiff must establish that an adequate warning would have convinced the treating physician not to prescribe the product for the plaintiff.[21]

To satisfy the burden of establishing warning causation, a plaintiff may introduce either objective evidence of how a reasonable physician would have responded to an adequate warning,[22] or subjective evidence of how the treating physician would have responded.[23] But, to create a jury question, the evidence introduced must be of sufficient weight to establish, by the preponderance of the

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[21] *Fortenberry*, 530 So.2d at 691; *see also Phillips v. Hull*, 516 So.2d 488, 493 (Miss. 1987); *Willett v. Baxter Int'l, Inc.*, 929 F.2d 1094, 1098-99 (5th Cir.1991); *Plummer v. Lederle Labs.*, 819 F.2d 349, 358-59 (2d Cir.), *cert. denied*, 484 U.S. 898, 108 S.Ct. 232, 98 L.Ed.2d 191 (1987); *Kirsch v. Picker Int'l, Inc.*, 753 F.2d 670, 671 (8th Cir.1985).

[22] *See, e.g., Hermes v. Pfizer, Inc.*, 848 F.2d 66, 69-70 (5th Cir.1988).

[23] *See Willett*, 929 F.2d at 1099; *Stanback v. Parke, Davis & Co.*, 657 F.2d 642, 645 (4th Cir.1981). The D.C. Circuit has required objective evidence to establish causation in a similar situation. *See Hartke v. McKelway*, 707 F.2d 1544, 1550-51 & n.6 (D.C.Cir.), *cert. denied*, 464 U.S. 983, 104 S.Ct. 425, 78 L.Ed.2d 360 (1983); *Henderson v. Milobsky*, 595 F.2d 654, 658-69 & n. 26 (D.C.Cir. 1978); *Canterbury v. Spence*, 464 F.2d 772, 791 (D.C.Cir.), *cert. denied*, 409 U.S. 1064, 93 S.Ct. 560, 34 L.Ed.2d 518 (1972).

evidence, at least some reasonable likelihood that an adequate warning would have prevented the plaintiff from receiving the drug.

B. *A Presumption of Causation?*

Accepting that she must prove that an adequate warning would have prevented her from receiving the drug, Thomas asks us to presume warning causation if a warning is inadequate, and cites in support of her presumption comments j and k of section 402A of the Restatement (Second) of Torts. In relevant part, comment j provides:

> Where warning is given, the seller may reasonably assume that it will be read and heeded; and a product bearing such a warning, which is safe for use if it is followed, is not in defective condition, nor is it unreasonably dangerous.[24]

In 1972, the Texas Supreme Court suggested in dicta that comment j could be read to create a rebuttable presumption in favor of a plaintiff that the plaintiff would have read and heeded a warning if it had been given.[25]

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[24] The "read and heed" aspect of this comment seems intended to preclude a finding of causation against a defendant in a products liability action so long as an adequate warning is given. Of course, as such, the "read and heed" aspect is superfluous. If an adequate warning is given, the product is not defective, and resolution of causation becomes irrelevant to liability.

[25] *See Technical Chemical Co. v. Jacobs*, 480 S.W.2d 602, 605 (Tex. 1972).

Building on this dicta, we predicted, in *Reyes v. Wyeth Laboratories*,[26] that Texas courts would adopt the following presumption:

> Where a consumer, whose injury the manufacturer should have reasonably foreseen, is injured by a product sold without a required warning, a rebuttable presumption will arise that the consumer would have read any warning provided by the manufacturer, and acted so as to minimize the risks.[27]

No Mississippi court has adopted a presumption of causation on facts similar to those in this case, and the failure of the Mississippi Supreme Court to mention such a presumption in *Fortenberry* strongly suggests that such a presumption does not exist under Mississippi law.

Furthermore, in attempting to predict the likely course that Mississippi law will take, we recognize that there are two very different types of warnings that might be associated with a particular product: (1) an unavoidable risk warning; and (2) a preventable risk warning. The first type of warning details a risk that a consumer[28] cannot avoid if the consumer chooses to use the product. Typically, warnings associated with medical drugs falls into this category. For example, a product description

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[26] 498 F.2d 1264 (5th Cir.), *cert. denied*, 419 U.S. 1096, 95 S.Ct. 687, 42 L.Ed.2d 688 (1974).

[27] 498 F.2d at 1281.

[28] The term "consumer" refers to the person making the decision whether a product should be used or purchased. In the context of a prescription drug, the term includes the learned intermediary who also invariably makes the decision whether to prescribe the drug.

may warn that one in four hundred thousand patients will suffer a certain adverse reaction. There is nothing that can be done about the risk, and often no way to discern in advance who will be the one person in four hundred thousand to experience the adverse reaction. The only question for the potential consumer of the product is whether the potential benefit to be obtained from using the product outweighs this risk. The second type of warning is customarily associated with mechanical products, and details risks that can be avoided by using the product in a certain manner.[29] For example, a pressurized can may warn users of the dangers of puncturing the can or of exposing the can to extremes of temperature. By heeding the warning, the consumer may use the product safely and avoid the detailed risks.

The *Reyes* presumption provides that a product user will read a warning and act to minimize his level of risk. Typically, the choice facing the user in the preventable risk situation is between using the product safely and using the product unsafely. Because the precautions are typically minimal (*ie.*, store the pressurized can away from the water heater), we have little trouble with a rebuttable presumption that a reasonable product user will choose to use the product safely. The choice, however, presented by an unavoidable risk warning is not between the safe use and the unsafe use of a product, but between using and not using the product. The consumer can choose to use the product and face its risks, or choose not to use the product and lose its potential benefits.

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[29] *See, e.g., Pavlides v. Galveston Yacht Basin, Inc.*, 727 F.2d 330, 338-39 (5th Cir.1984).

Generally, using the product will present the less risky of these two alternatives. Consider the polio vaccine in *Reyes*. There is a risk of contracting polio if a person uses the vaccine, and there is a risk if the person decides not to use the vaccine. Presumably, the risk of contracting polio is less with the vaccine than without it. If we assume that the average user will take the less risky alternative, the average user will choose to take the vaccine, and a warning detailing the unavoidable risks of the polio vaccine, whether given or not, would not change the decision.[30] Unless the plaintiff can establish that using the product is, for the average consumer, the more risky alternative, the *Reyes* rule that the consumer will act to minimize his level of risk, if applied in the context of an unavoidable risk, would seem to establish a rebuttable presumption that the consumer would not have changed his decision to use the product if warned of the unavoidable risk.

For this reason, we reject Thomas's contention that causation is presumed, given an inadequate warning, in the context of an unavoidable risk. We are willing to assume that the failure to give an adequate warning of a known risk entitles the plaintiff to a rebuttable presumption that the learned intermediary would have read and heeded a proper warning. But "heed" in this context means only that the learned intermediary would have

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[30] In *Reyes*, we assumed that there was something the plaintiff could have done to reduce the risk of contracting polio from the vaccine. *Reyes*, 498 F.2d at 1281-82 ("Perhaps this [warning] would have prevented her polio.").

incorporated the "additional"[31] risk into his decisional calculus.[32] The burden remains on the plaintiff to demonstrate that the additional non-disclosed risk was sufficiently high that it would have changed the treating physician's decision to prescribe the product for the plaintiff.[33]

In summary, in a failure to warn case involving a prescription drug, Mississippi law requires a plaintiff to establish that an adequate warning would have prevented the plaintiff's injury. To establish that element, the plaintiff must establish, by the preponderance of the evidence, both: (1) that an adequate warning would have prevented the treating physician from administering the drug; and (2) that the injury would not have occurred had the drug not been administered.

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[31] Because it is uncertain whether the seizures were coincidental or causally related to the taking of Accutane, it is uncertain whether there was, in fact, any additional risk to be disclosed. At best, there was the possibility of an additional risk.

[32] While we recognize that we reached the opposite result in *Reyes*, we do not follow that decision for two reasons: (1) we decided that case under Texas law, and we are deciding this case under Mississippi law; and (2) despite the opportunity, Texas courts have not adopted the *Reyes* presumption in unavoidable risk cases. *See Cooper v. Bowser*, 610 S.W.2d 825, 832-33 (Tex.Civ.App. – Tyler 1980, no writ).

[33] Instead of addressing the issues of warning inadequacy and warning causation separately, we could have combined the inquires by defining the duty of a drug manufacturer to warn as requiring a warning only of those risks sufficiently serious that they would affect the average physician's decision to use the product. *See* P. Keeton, D. Dobbs, R. Keeton, D. Owen, *Prosser and Keeton on Torts* § 42, at 274-75 (5th ed. 1984).

III. SUFFICIENCY OF THE EVIDENCE

In reviewing a judgment notwithstanding the verdict, we view the evidence in the light most favorable to the non-moving party.[34] If, in that light, a reasonable jury cannot find an essential element of the plaintiff's case, that we will affirm the judgment notwithstanding the verdict in favor of the defendant.[35]

Warning Causation: Sufficiency of the Evidence.

In his testimony, Dr. O'Donnell testified that the actual warning given was inadequate, and rendered Accutane unreasonably dangerous, for two reasons: (1) Hoffman-LaRoche failed to send a "Dear Doctor" letter to all physicians detailing the available information on the reported seizures in the fall of 1983; and (2) Hoffman-LaRoche failed to contraindicate use of Accutane for all patients except those suffering from severe cystic acne.[36]

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[34] *Boeing Co. v. Shipman*, 411 F.2d 365, 375 (5th Cir. 1969) (en banc).

[35] *See, e.g., Broch v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 308-09 (5th Cir.), *modified on other grounds on rehearing*, 884 F.2d 166 (5th Cir.1989), *cert. denied*, ___ U.S. ___, 110 S.Ct. 1511, 108 L.Ed.2d 646 (1990).

[36] Because Accutane is chemically related to Vitamin A, Dr. O'Donnell testified that the warning was also inadequate because Hoffman-LaRoche failed to list all of the potential side effects of Vitamin A. Hoffman-LaRoche did state that Accutane was related to Vitamin A, but it did not list all the known potential side effects of Vitamin A. While the potential side effects of a related chemical may be important in the early stages of a drug, by January of 1984, over 400,000 patients had

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Before we address the warning causation issue, we consider whether the evidence in the record will support a reasonable jury finding that Accutane was unreasonably dangerous in the absence of these two additional warnings.

1. *A Reasonable Warning*

Mississippi law requires a manufacturer to give a reasonable warning.[37] To be reasonable, the warning should neither understate nor overstate the known risks associated with the use of a particular product. We consider whether a reasonable jury could have found either aspect of the warning recommended by Dr. O'Donnell to be reasonable under the circumstances of this case.

The undisputed evidence establishes that, by the end of January 1984, ten patients had reported seizures during their treatment with Accutane. At trial, all of the plaintiff's experts agreed that the seizures experienced by nine of the ten patients were eventually determined to be

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taken Accutane. With this many patients, listing the actual side effects reported by Accutane patients provides a much better indication of the risks associated with Accutane, than would a list of the side effects of Vitamin A. Indeed, listing the side effects of Vitamin A, even though they had not been observed in these 400,000 patients, would tend to overstate the risks associated with Accutane. For that reason, we hold that Accutane was not unreasonably dangerous, as a matter of law, in January of 1984, for failing to list those side effects of Vitamin A that had not been reported or observed in the Accutane patients.

[37] *Fortenberry*, 530 So.2d at 692.

unrelated to the taking of Accutane, and that the tenth most likely involved a fainting spell.[38] (It remained uncertain whether the tenth reported incident was caused by the taking of Accutane.) The evidence also suggested that the Accutane patients had fewer seizures than would have been expected, on average, due to the background risk of seizures in the general population.

Based on the available evidence, a reasonable jury could determine that there was at least the possibility that seizures were caused by Accutane in very rare cases. We assume, but do not decide, that a reasonable jury could have found the warning accompanying Accutane to be inadequate for failing to provide information on this possibility.

With regard to the reasonableness of Dr. O'Donnell's recommended contraindiction, we find insufficient evidence to support a finding that Accutane was unreasonably dangerous absent such contraindication. As Dr. O'Donnell and several other expert witnesses testified, a statement that a particular use is contraindicated does much more than a typical warning. Where a typical warning lists possible side effects and their likelihood, permitting the treating physician to balance the potential costs and benefits in a particular situation, a contraindication is

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[38] Of the ten reported seizures, three involved patients with a prior history of seizures, three involved patients who were diagnosed as having epilepsy unrelated to Accutane, one involved a patient who was eventually diagnosed as having a pre-existing seizure disorder, and two involved patients whose physicians specifically determined that the seizures were not related to Accutane. The tenth report involved a fainting spell, and no cause was determined.

essentially a direction to the physician not to use the drug in certain circumstances. When a use is contraindicated, the manufacturer and the FDA have already balanced the costs and benefits of the drug and determined that, under the stated conditions, the risks of using the product will always outweigh the benefits. As all of the witnesses agreed, a physician will not prescribe a product when its use is contraindicated, absent exceptional circumstances.

In order to justify a particular contraindication, a plaintiff must introduce evidence that the risks of the drug will almost always outweigh its benefits in the situation contraindicated. The only evidence that the risks of Accutane outweighed its benefits for all patients except those with severe cystic acne comes from Dr. O'Donnell. He testified that the use of Accutane should have been contraindicated in all cases other than severe cystic acne. In essence, he is testifying that the risks of Accutane outweigh its benefits for everyone other than a patient with severe cystic acne. Two undisputed facts stand in sharp contrast to Dr. O'Donnell's opinion.

First, the FDA, after considering all of the evidence, provided a contraindication only for "patients who are pregnant or who intend to become pregnant while undergoing treatment" and for "patients who are sensitive to parabens". Despite knowledge of the risks associated with Accutane, the FDA did not consider it so risky as to require a contraindication for all patients except those with sever cystic acne. Instead, the FDA decided to leave that decision to the individual physician in each particular case. Second, the undisputed testimony at trial established that over one million patients had used Accutane, and that at most only 360,000 persons in the United States

suffer from cystic acne.[39] Thus, despite the risks of Accutane, it is undisputed that thousands of physicians prescribed Accutane for patients who did not suffer from severe cystic acne.

In resolving this issue, we cannot avoid the fact that the products liability system plays a dual role of compensating injured victims and regulating products. If we permit the subjective opinion of a single expert to create a genuine issue of material fact in the face of the decisions of the FDA and thousands of physicians so that a particular plaintiff can recover, we would be denying access to Accutane for hundreds of thousands of acne sufferers.[40]

In *Matsushita Electric Industrial Co v. Zenith Radio Corp*,[41] the Supreme Court addressed a similar issue. In *Matsushita*, the Court held that there was insufficient evidence to create a jury issue on the existence of a predatory pricing conspiracy despite expert testimony that such a conspiracy could and did exist.[42] Because the undisputed historical evidence from the market established that such a conspiracy would be unprofitable, the

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[39] It is unclear how many of the 360,000 suffered from severe cystic acne.

[40] Alternatively, and perhaps worse, we would force drug manufacturers to list, and perhaps contraindicate, every possible risk in order to avoid the possibility of liability. If manufacturers so respond to the possibility of liability, physicians will begin to ignore or discount the warnings provided by the drug manufacturers. Permitting a jury to find liability on such a basis would undermine the important role of warnings as a device to communicate vital information to physicians.

[41] 475 U.S. 574, 106 S.Ct. 1348, 89 L.Ed.2d 538 (1986).

[42] 475 U.S. at 593-95 & n. 19, 106 S.Ct. at 1359-60 n. 19.

Court held the expert testimony insufficient to create jury issue.[43] The Court feared that to permit the case to go to the jury in the face of the market evidence would discourage competition,[44] either because the actual jury might reach an unreasonable result, or because of the high cost of convincing the jury to reach the right answer.[45]

We find this analysis fully applicable to this case. Thousands of physicians, and hundreds of thousands of patients, have judged Accutane to be worth the risk, even after the possible seizure risk was disclosed. Because this balancing decision is inescapably a personal one,[46] the

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[43] 475 U.S. at 588-93 & 595-97, 106 S.Ct. at 1356-59, 1360-61.

[44] 475 U.S. at 593-94, 106 S.Ct. at 1359-60; *see also Monsanto Co. v. Spray-Rite Serv. Corp.*, 465 U.S. 752, 762-64, 104 S.Ct. 1464, 1470-71, 79 L.Ed.2d 775 (1984).

[45] As a third possibility, the Court might have been recognizing that most litigation is settled before a jury actually decides the case. Because of the uncertainty inherent in a jury verdict, permitting a case to go to a jury will substantially increase the settlement value of a case, even if, more often than not, the average jury will decide the case correctly. By taking the case from the jury, the Court removes that uncertainty and encourages conduct that it sees as likely to encourage, rather than discourage, competition.

[46] It is simply not possible to compare in any meaningful manner the pain suffered by those few who experience an adverse reaction with the joy of the many who are cured of their acne. Whether the possibility of a cure is worth the risk of an adverse reaction is a balancing decision most appropriately left to the individual patient and the treating physician. When the relevant risks and benefits are disclosed, these two are best placed to decide whether the gamble of a particular treatment is worth the risk for a particular patient.

opinion of Dr. O'Donnell that Accutane is not worth the risk is insufficient to create a genuine issue of fact in the face of these informed decisions. We, therefore, hold, as a matter of law, that the failure to include the recommended contraindication did not render the warning inadequate.

2. *Warning Causation*

Assuming that the failure to inform physicians of the possibility of seizures in the fall of 1983 rendered Accutane unreasonably dangerous, we now consider whether Thomas has introduced sufficient evidence to permit a reasonable jury to find that an adequate warning would have prevented Thomas's injuries. Dr. O'Donnell expressed no opinion on whether a warning concerning the possibility of a seizure risk, in the absence of his recommended contraindication, would have changed the decision of a reasonable physician to prescribe Accutane for Thomas. The careful wording of his first attempt at the warning causation issue strongly suggests that his opinion was based on the contraindication aspect of his recommended warning. Without the contraindication included in the warning, we cannot be certain that Dr. O'Donnell would have expressed the same opinion on the warning causation issue. We are not overly concerned, though, with what opinion Dr. O'Donnell might have expressed on this issue because, in examining the remainder of the record, we find evidence that eliminates any reasonable possibility that the release of the information concerning the ten reported seizures would have changed the decision of Dr. Myers to prescribe Accutane in this case.

It is undisputed that Thomas suffered from a serious acne condition. She had been under treatment for her condition for over seven years. While it is probable, though not entirely certain, that she was suffering from cystic acne when she went to Dr. Myers in January of 1984, it is certain that her acne was not responding to conventional therapy, including systemic antibiotics. Furthermore, there was nothing in Thomas's prior history to suggest that she would be the one person in so many thousands to suffer an adverse reaction to Accutane. Thus, Thomas was a reasonable, though perhaps not ideal, choice for treatment with Accutane.

In the spring of 1984, Hoffman-LaRoche disclosed the available information on the reported seizures to physicians. Yet, even after the release of this information, Accutane has remained a popular choice for acne treatment. Indeed, it appears from the record that the release of the seizure information had no effect on the overall level of Accutane use.[47] Since the seizure warning in 1984, physicians have prescribed Accutane for hundreds of thousands of patients, the vast majority of whom were, like Thomas, reasonable, though perhaps not ideal, candidates for Accutane treatment. Furthermore, Thomas has failed to introduce evidence of even a single physician who actually changed his or her practice concerning Accutane based on the release of the seizure information.

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[47] This is not surprising given that the risk of seizures for those taking Accutane was, from our perspective, indistinguishable from the background risk of seizures for the general population.

We hold that this undisputed historical evidence concerning the usage of Accutane after an adequate seizure warning was given precludes any reasonable possibility that information on the ten reported seizures would have prevented Thomas's injury. The possibility that Dr. Myers would have changed his decision if he had been warned of the possibility of rare seizures caused by Accutane is too remote to create a genuine issue of fact with respect to warning causation.[48] Because of the failure of the plaintiff to establish causation, we must affirm the judgment notwithstanding the verdict.[49]

IV. CONCLUSION

We hold that under Mississippi law a plaintiff in a prescription drug failure to warn case must establish, by a preponderance of the evidence, that the inadequate warning caused the plaintiff's injuries. The plaintiff must show that an adequate warning would have convinced the prescribing physician not to prescribe the drug for the plaintiff. No reasonable jury could conclude that Dr. Myers would not have prescribed Accutane for Thomas. We AFFIRM the judgment notwithstanding the verdict granted by the district court. Because of our affirmance of the district court's decision as to the adequacy of the warning, we need not address the drug causation issue.

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[48] *Cf. Willett*, 929 F.2d at 1099.

[49] *See Willett*, 929 F.2d at 1099; *Plummer v. Lederle Labs.*, 819 F.2d at 358-59; *Kirsch v. Picker Int'l, Inc.*, 753 F.2d at 671; *Stanback v. Parke, Davis & Co.*, 657 F.2d at 645.

APPENDIX B

Order Denying Rehearing, dated 25 February 1992.

IN THE UNITED STATES COURT OF APPEALS
FOR THE FIFTH CIRCUIT

No. 89-4908

MARY KATHRYN THOMAS,

Plaintiff-Appellant,

versus

HOFFMAN-LAROCHE, INC.,

Defendant-Appellee.

Appeal from the United States District Court for the Northern District of Mississippi

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ON PETITION FOR REHEARING AND SUGGESTION FOR REHEARING EN BANC

(Opinion 01/03/92, 5 Cir., 1992, ___ F.2d ___)

(February 25, 1992)

Before WISDOM, KING and BARKSDALE, Circuit Judges.

PER CURIAM:

(X) The Petition for Rehearing is DENIED and no member of this panel nor judge in regular active service on the Court having requested that the Court be polled on rehearing en banc, (Federal Rules of Appellate Procedure and Local Rule 35) the suggestion for Rehearing En Banc is DENIED.

( ) The Petition for Rehearing is DENIED and the Court having been polled at the request of one of the members of the Court and a majority of the Circuit Judges who are in regular active service not having voted in favor of it, (Federal Rules of Appellate Procedure and Local Rule 35) the Suggestion for Rehearing En Banc is also DENIED.

( ) A member of the Court in active service having requested a poll on the reconsideration of this cause en banc, and a majority of the judges in active service not having voted in favor of it, rehearing en banc is DENIED.

ENTERED FOR THE COURT:

/s/ John Minor Wisdom
United States
Circuit Judge

CLERK'S NOTE:
SEE FRAP AND LOCAL RULES 41 FOR STAY OF THE MANDATE